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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/548,081	04/12/00	DORWALD	F 5390.200-US

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EXAMINER

LIU, H

ART UNIT	PAPER NUMBER
1624	<i>Q</i>

DATE MAILED: 05/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.
09/548,081

Applicant(s)

Dorwald et al.

Examiner

Hong Liu

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above, claim(s) 4, 45, 47, and 49-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-44, 46, and 48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 and 5 20) ☐ Other: _____

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DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-3, 5-63, drawn to the compounds of formula I wherein $m=n=p=0$, $q=1$, their compositions and one method of use, classified in class 546, subclass 118.
 - II. Claims 1, 2, 4-63, drawn to the compounds of formula I wherein $n=p=0$, $m=q=1$, their compositions and one method of use, classified in class 540, subclass 578
 - III. Claims 1-63, drawn to the compounds, composition, and methods of use not included in Group I, classified in classes and subclasses depending on the nature of the substituents.

The inventions are distinct, each from the other because of the following reasons:

Groups I-III are directed to structurally dissimilar compounds such that the variable core created by varying the definitions of the formula do not belong to a recognized class of chemical compounds in the art, and references anticipating one invention would not render obvious the others, for example, imidazo[4,5-d]azepine is different from imidazo[4,5-d]pyridine. Thus, separate searches in the literature as well as in the U.S. Patent Clarification System would be required. Each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structures as functional equivalents of each other. The

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mere fact that there is a single similarity is not in itself a significant reason to render the whole embodiment obvious.

Inventions I and III also are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case more than one use exists for compounds of Group I as evidenced by claims 45-63 drawn to a variety of diverse uses. Additionally, the various uses would raise issues of enablement separate from that of the compound claims and would require art-recognized evidence that activity relied on its reasonably correlated to in vivo efficacy for the uses claimed.

During a telephone conversation with Ms. Reza Green on 04/20/01 a provisional election was made with traverse to prosecute the invention of Group 1, claims 1-3, 5-44, along with claims 46 and 48. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4, 45, 47, and 49-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

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amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

3.

Improper Markush Grouping

Claims 1, 2, 5-44, 46, and 48 are rejected under judicially created doctrine as being an improper Markush grouping. The recited compounds, while possessing a common utility, present a variable core and, thus, the Markush groups represented by the term wherein $m=n=p=0$, $q=1$ and $n=p=0$, $m=q=1$ have variably different definitions, render the claims clearly improper.

Deletion of non-elected subject matter would overcome this rejection.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed on April 12, 2000. It is noted, however, that applicant has not filed a certified copy of the priority document as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-3, 5-44, 46, and 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following reason(s) apply:

The claims are not commensurate in scope as to the possibilities for the substituent “heteroarylmaino”, “heteroaryl”, “heteroaroyl” in the various R definitions. The specification has no specific definition for these terms except some examples and, therefore, they are open-ended and all encompassing. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these broad claims, which embrace a diversity of hetero and aryl rings at various locations on the imidazo[4,5-d]pyridine.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein X, Y, A can be a bond and other variables. And Rs can be an unsubstituted or substituted, single or fused, aromatic or an unsubstituted or substituted, fused or single, heteroaromatic group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional “H3 receptor antagonists” which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants’ claims. Only compounds wherein R5 and R6 are hydrogens, A is a bond, alkyl, R3 or R4 is hydrogen, methyl, alkyl-substituted phenyl, spiro, alkyl have been made.

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Furthermore, no testing data is provided for any of the compounds listed in the specification. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R variables on the imidazo[4,5-d]pyridine ring system embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the “working examples” fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch*, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention.

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Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability” have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

In claim 1, R1 is defined as a functional group which can be converted to hydrogen *in vivo*. The scope of a functional group which can be converted to hydrogen *in vivo* is not adequately enabled. Applicants provide no guidance as how the compounds are made more active *in vivo*. The choice of a “a functional” will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrug will be suitable for the instant invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-44, 46, and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

7. 1). The use of “heteroaryl” and “heteroaroyl” in the definition of R variables is unclear to the array of heteroatoms, size of the rings, as well as nature of atoms as ring members. See *In re Wiggins* 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.

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2). Claim 1 is vague and indefinite in that it recites the compounds “as well as its pharmaceutically acceptable salts...” It is not clear whether the claim is drawn to an instantly claimed compound or a mixture . The word “or” is suggested in place of “as well as”.

3). Original claim 14 is not dependent on a preceding claim. Clarification is required.

8. 4). Claims started with “a medicament of...” are not usual composition claims. Revision of these claims to comply with the normal US claim format is suggested. In addition, some of these claims differ from other composition claims only in terms of indented use. The claims would be rejected as duplicate claims since intended use is not given material weight. Note In re Tuominen 213 USPQ 89.

Specification

9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1-3, 5, 7-11, 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Remelli et al., Chem Abstract 128: 75655. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 200575-98-0 and 200575-98-0. *amended by proviso*

Claims 1-3, 5, 7-11, 20, 33-44, 46, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Krause et al. (J. Med. Chem., 1995). Krause teaches the compounds, compositions and methods of use of the instant invention (see Compound 11 on page 4072). *overcome*

Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Arcari et al. (DE 2700012). Arcari teaches the compounds and composition of the instant invention (see Examples 19-25, 50, 51, 60, and 61). *not overcome*

Claims 1-3, 7-14, 18, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hauck et al., Chem Abstract 92: 146611. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 72717-36-3. *Not overcome*

Claims 1-3, 7-14, 18, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Yutilov et al., Chem Abstract 99: 70725. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 86674-44-4. *not overcome*

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Claims 1-3, 5-15, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Scarponi et al. (GB 2158440). Scarponi teaches the compounds and composition of the instant invention (see Examples 2, 3, 9, and 10). *overcome*

Claims 1-3, 5-15, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Stocker et al., Chem Abstract 112: 216653. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *proviso*

Claims 1-3, 5-15, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Klutchko et al., Chem Abstract 114: 229317. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *proviso*

Claims 1-3, 5-13, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Vincent et al., Chem Abstract 117: 251781. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *not argued.*

Claims 1-3, 5-15, 20-23, 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Clarke et al. (WO 92/18115). Clarke teaches the compounds and composition of the instant invention (see the first example of preferred compounds on page 20). *overcome*

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Claims 1-3, 5-15, 20-23, 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Enari et al. (EP 589665). Enari teaches the compounds and composition of the instant invention (see the examples and the attached CAS printout). *provided*

Claims 1-3, 5-15, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al., Chem Abstract 126: 104085. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *provided*

Claims 1-3, 5, 7-15, 20-23, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Thorwart et al., Chem Abstract 127: 65701. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *provided*

Claims 1-3, 5, 7-11, 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Casella et al. (J. Am. Chem. Soc., 1881). Casella teaches the compounds of the instant invention (see compounds on page 6340). *overcome*

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arcari et al. (DE 2700012). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 1 wherein X can be NR₄ where NR₄ is hydrogen, an alkyl having from 1 to 4 carbon atoms, cyano, amino, R₂ is hydrogen, alkyl, cycloalkyl, phenyl, or heterocycle, R₃ is hydrogen, alkyl, cycloalkyl, phenyl etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole, i.e., pharmaceutical agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. V. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

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Claims 1-3, 5-15, 20-23, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scarponi et al. (GB 2158440). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 1 wherein R6 and R7 together with the nitrogen atom form a five or six membered hetero ring, R5 represents the group, R5 is -C(O)R2, -C(O)OR2, or c(Y)NH-R6, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole, i.e., pharmaceutical agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Claims 1-3, 5-17, 20-24, 27-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Honma et al. (EP 0531874). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 3 wherein R1 is hydrogen or lower alkyl, R2 is hydrogen, lower alkylsulfonyl group or a group of the formula C(Z)R⁰ wherein Z is an oxygen and R⁰ is alkyl, alkoxy or heterocyclic, etc. The compounds are taught to

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be useful as a pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole, i.e., pharmaceutical agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.


Claims 1-3, 5-15, 20-23, 29-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kureha et al. (EP 0589665). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 3 wherein R1 is hydrogen or, R2 is carbamoyl, R3 represents alkyl substituted phenyl, etc. The compounds are taught to be useful as a pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole, i.e., pharmaceutical

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Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for this group is (703) 308-4734 for "unofficial" purposes and the actual number for **official** business is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose number is (703) 308-1235.

hl
April 23, 2001


Mukund Shah
Supervisory Patent Examiner
Art Unit 1624